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		<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR</i>	
<input type="checkbox"/>	L1	smith.in. and helicobacter.ti,ab,clm.	51
<input type="checkbox"/>	L2	L1 and (freunds or cfa or ifa)	4
<input type="checkbox"/>	L3	l1 and douglas	7

END OF SEARCH HISTORY

20040052799. 30 Dec 02. 18 Mar 04. Nucleic acid and amino acid sequences relating to Helicobacter pylori for diagnostics and therapeutics. Smith, Douglas, et al. 424/184.1; A61K039/00 A61K039/38.

☐ 2. WO009921959A2. 28 Oct 98. 06 May 99. HELICOBACTER PYLORI VACCINE FORMULATIONS. ELLIS, RONALD W, et al. C12N00/;.

☐ 3. WO009824475A1. 05 Dec 97. 11 Jun 98. NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO HELICOBACTER PYLORI AND VACCINE COMPOSITIONS THEREOF. SMITH, DOUGLAS, et al. A61K039/00; C12Q001/68 A01N043/04.

☐ 4. WO009818323A1. 28 Oct 97. 07 May 98. NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO HELICOBACTER PYLORI AND VACCINE COMPOSITIONS THEREOF. SMITH, DOUGLAS, et al. A01N043/04; A61K031/70 C12Q001/68.

☐ 5. WO009737044A1. 27 Mar 97. 09 Oct 97. NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO HELICOBACTER PYLORI AND VACCINE COMPOSITIONS THEREOF. SMITH, DOUGLAS, et al. C12Q001/68; A01N043/04 A61K031/70.

☐ 6. WO009719098A1. 15 Nov 96. 29 May 97. NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO HELICOBACTER PYLORI FOR DIAGNOSTICS AND THERAPEUTICS. SMITH, DOUGLAS H. C07H021/04;.

☐ 7. WO009640893A1. 06 Jun 96. 19 Dec 96. NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO HELICOBACTER PYLORI FOR DIAGNOSTICS AND THERAPEUTICS. SMITH, DOUGLAS, et al. C12N015/00;.

*File 348: For important information about IPCR/8 and forthcoming changes to the IC= index, see HELP NEWSIPCR.
 File 340:CLAIMS(R)/US Patent 1950-06/Jul 27
 (c) 2006 IFI/CLAIMS(R)
 *File 340: IPCR/8 classification codes now searchable in 2006 records.
 For important information about IC=index changes, see HELP NEWSIPCR.
 File 654:US Pat.Full. 1976-2006/Jul 27
 (c) Format only 2006 Dialog
 *File 654: IPCR/8 classification codes now searchable in 2006 records.
 For information about IC= index changes, see HELP NEWSIPCR.

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1/3,KWIC/1 (Item 1 from file: 349)
 DIALOG(R)File 349:PCT FULLTEXT
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COLOURED FUSION PROTEINS
 PROTEINES HYBRIDES COLOREES

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 designated states except: US)

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200542748 A1 20050512 (WO 0542748)
 Application: WO 2004GB3543 20040818 (PCT/WO GB04003543)
 Priority Application: GB 200323897 20031011

Designated States:

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 2004+)

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 DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO
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 (EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PL PT RO
 SE SI SK TR
 (OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
 (AP) BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW
 (EA) AM AZ BY KG KZ MD RU TJ TM

CLAIMS B	(German)	200547	612
CLAIMS B	(French)	200547	708
SPEC B	(English)	200547	5196
Total word count - document A			0
Total word count - document B			7129
Total word count - documents A + B			7129

METHODS FOR PRODUCING ENHANCED ANTIGENIC %HELICOBACTER% SP. AND VACCINES
COMPRISING SAME

METHODES DE PRODUCTION D'%HELICOBACTER% SP. ANTIGENE AMELIORE ET DE VACCINS
LE CONTENANT

...SPECIFICATION Campylobacter jejuni proteins expressed in vivo.

The NCBI Taxonomy browser identifies that Campylobacter pylori and
%Helicobacter% pylori are synonymous.

Therefore, objects of the present invention include 1) in vitro culture
conditions...

...THE INVENTION

This invention provides defined culture conditions and components
incorporated into growth media of %Helicobacter% pylori or %Helicobacter%
felis to induce or enhance the presence of virulence factors and other
antigens. Preferably, such...

...as passive vaccines.

Therefore, an aspect of the present invention is a method for producing
%Helicobacter% pylori or %Helicobacter% felis according to claim 1.

A further aspect of the invention is %Helicobacter% pylori or
%Helicobacter% felis according to claim 4.

Another aspect of the invention is a vaccine according to...

...Figure 1 graphically depicts the effect of bile concentration and the
growth phase of the %Helicobacter% pylori culture on the adhesiveness of
%Helicobacter% pylori NB3-2 cells. H. pylori NB3-2 cells were grown in
culture medium containing...

...Figure 2 graphically depicts the effect of bile concentration and the
growth phase of the %Helicobacter% pylori culture on the adhesiveness of
%Helicobacter% pylori G1-4 cells. H. pylori G1-4 cells were grown in
culture medium containing...

...5 DETAILED DESCRIPTION OF THE INVENTION

The methods of the present invention relate to growing %Helicobacter%
pylori or %Helicobacter% felis bacteria in vitro in the presence of a
combination of certain conditions with certain...

...skilled in the art and maintained at -80(degree)C for future use. Stocks
of %Helicobacter% pylori can be prepared by growing the organism in brain
heart infusion broth ("BHI"). Bacteria...

...in the art, such as by centrifugation.

In further preferred embodiments, antigenically enhanced cells of
%Helicobacter% pylori, preferably of the strain ATCC 49503, NB3-2 or
G1-4, are grown in...for production of antigenically enhanced bacteria
correlate to enhanced virulence in small animal models. With
%Helicobacter% pylori, the %Helicobacter% felis gastric colonization
model described by Chen et al. (Lancet, 339:1120-1121, 1992) is...

...present invention are described below.

6 EXAMPLES: METHODS FOR PRODUCING ENHANCED ANTIGENIC BACTERIA

Example 1. %Helicobacter% pylori was added to BHI broth plus 4% bovine
calf serum. After inoculation the flasks...

...24 h at 37(degree)C. The cells were harvested as described above.

Example 2. *Helicobacter* pylori was added to BHI broth plus 4% bovine calf serum. After inoculation the flasks...

...when the culture of each strain was in log phase growth.

EXAMPLE: VACCINE EFFICACY OF *HELICOBACTER* GROWN ACCORDING TO THE METHODS OF THE PRESENT INVENTION

Example 4. The protective efficacy of formalin-fixed whole cell *Helicobacter* pylori grown according to the methods of the present invention was determined using the mouse *Helicobacter* felis gastric colonization model described by Chen et al. (Lancet, 339:1120-1121, 1992). *Helicobacter* pylori strain G1-4 was grown as a seed culture for about 22 h at...

...of this inactivated whole cell vaccine orally to 6-8 week old female Balb/c *Helicobacter*-free mice at days 0, 7 and 14 or at days 0, 7 and 21...

...was taken as a positive urease result.

As shown in Table 20, administration of enhanced *Helicobacter* whole cell vaccine prepared using *H. pylori* strain G1-4 protected animals against an *H.*

...CLAIMS B1

1. A method of producing *Helicobacter* pylori or *Helicobacter* felis bacteria having enhanced antigenic properties which comprises growing a culture of the *Helicobacter* bacteria in vitro in brain heart infusion broth culture medium supplemented with bovine calf serum...

...immunogenic antigen when compared to the antigenic property of bacteria from a culture of the *Helicobacter* species in brain heart infusion broth supplemented with bovine calf serum.

2. The method according...

...comprise 0.05% glycocholate bile salt.

3. The method according to claim 3, wherein said *Helicobacter* is *Helicobacter* pylori strain, NB3-2 having ATCC Accession No. 55714 or G1-4 having ATCC Accession No. 55713.

4. A *Helicobacter* pylori or *Helicobacter* felis bacterium having enhanced antigenic properties, which is obtainable by culturing *Helicobacter* bacteria in vitro in brain heart infusion broth culture medium supplemented with bovine calf serum...

...immunogenic antigen when compared to the antigenic property of bacteria from a culture of the *Helicobacter* species in brain heart infusion broth supplemented with bovine calf serum.

5. The *Helicobacter* bacterium according to claim 4, wherein said conditions comprise 0.05% sodium glycocholate.

6. The *Helicobacter* bacterium according to claim 4, wherein said *Helicobacter* is *Helicobacter* pylori strain, NB3-2 having ATCC Accession No. 55714 or G1-4 having ATCC Accession No. 55713.

7. A vaccine comprising the *Helicobacter* bacterium of claim 4, and further comprising pharmaceutically acceptable carrier or diluent.

8. The vaccine according to claim 7, wherein said *Helicobacter* bacterium is inactivated.

9. The vaccine according to claim 8, wherein said *Helicobacter* bacterium is inactivated by formalin treatment.

10. The vaccine according to claim 7, wherein said...

...comprising an adjuvant.

12. A method for assaying a potential antimicrobial agent comprising, contacting the *Helicobacter* bacterium of claim 4 in vitro with said agent and assaying the bacteriocidal or bacteriostatic effects of said agent on the *Helicobacter* bacterium.

- 13. A method for detecting a host's antibodies to %Helicobacter% bacteria in an animal or biological sample therefrom, comprising the steps of a) contacting said biological sample with the %Helicobacter% bacterium of claim 4 in vitro and b) screening for antibody binding of the %Helicobacter% bacterium or fragment thereof.
- 14. A diagnostic immunoassay kit for detecting a host's production of antibodies to %Helicobacter% bacteria or for detecting %Helicobacter% bacteria, comprising the %Helicobacter% bacterium of claim 4.
- 15. A method for producing anti-%Helicobacter% antibodies in a non-human animal which comprises using an effective amount of an immunogen comprising the %Helicobacter% bacterium of claim 4, wherein the anti-%Helicobacter% antibodies bind said %Helicobacter% bacterium or a component thereof.
- 16. An immunogen comprising the %Helicobacter% bacterium of claim 4, for stimulating an immune response in an animal wherein said immunogen is to be administered to the animal and said immune response prevents, attenuates or cures %Helicobacter% infections or diseases in the animal.

...CLAIMS B1

- 1. Eine Methode zur Produktion der Bakterien %Helicobacter% pylori oder %Helicobacter% felis mit verstärkten Antigeneigenschaften, umfassend das Anlegen einer in vitro-Kultur der %Helicobacter%-Bakterien in Brain Heart Infusion Broth Kulturmedium, das mit bovinem Kalberserum aufgestockt wurde, unter einer...

...Vergleich mit der antigenen Eigenschaft von Bakterien einer mit bovinem Kalberserum aufgestockten Kultur der Spezies %Helicobacter% in Brain Heart Infusion Broth eine höhere Stufe eines immunogenen Antigens oder eines neuen immunogenen...

...Bedingungen 0,05% Gallen-Glykocholat umfassen.

- 3. Die Methode gemas Anspruch 3, worin der genannte %Helicobacter% der Stamm %Helicobacter% pylori ist und wobei NB3-2 die ATCC-Zugriffs-Nr. 55714 oder G1-4 die ATCC-Zugriffs-Nr. %55713% hat.
- 4. Ein %Helicobacter% pylori- oder %Helicobacter% felis-Bakterium mit verstärkten antigenen Eigenschaften, das man produzieren kann, indem in vitro Kulturen von %Helicobacter%-Bakterien in Brain Heart Infusion Broth Kulturmedium, das mit bovinem Kalberserum aufgestockt wurde, unter einer...

...Vergleich mit der antigenen Eigenschaft von Bakterien einer mit bovinem Kalberserum aufgestockten Kultur der Spezies %Helicobacter% in Brain Heart Infusion Broth eine höhere Stufe eines immunogenen Antigens oder eines neuen immunogenen Antigens darstellt.

- 5. Das %Helicobacter%-Bakterium gemas Anspruch 4, worin die genannten Bedingungen 0,05% Natriumglykocholat umfassen.
- 6. Das %Helicobacter%-Bakterium gemas Anspruch 4, worin der genannte %Helicobacter% der Stamm %Helicobacter% pylori ist und wobei NB3-2 die ATCC-Zugriffs-Nr. 55714 oder G1-4 die ATCC-Zugriffs-Nr. %55713% hat.
- 7. Ein Impfstoff, umfassend das %Helicobacter%-Bakterium gemas Anspruch 4 und weiterhin umfassend einen pharmazeutisch akzeptablen Trägerstoff oder Diluenten.
- 8. Der Impfstoff gemas Anspruch 7, worin das genannte %Helicobacter%-Bakterium inaktiviert wurde.
- 9. Der Impfstoff gemas Anspruch 8, worin das besagte %Helicobacter%-Bakterium durch Formalin-Behandlung inaktiviert wurde.
- 10. Der Impfstoff gemas Anspruch 7, wobei sich der...

...12. Eine Assay-Methode für einen potentiellen antimikrobiellen Wirkstoff, umfassend den in vitro-Kontakt des %Helicobacter%-Bakteriums gemas Anspruch 4 mit dem genannten Wirkstoff und die Ermittlung der bakteriziden und bakteriostatischen Effekte des besagten Wirkstoffs auf das %Helicobacter%-Bakterium.

- 13. Eine Methode zur Detektion der Wirtsantikörper gegen %Helicobacter%

-Bakterien in Proben von Lebewesen oder in biologischen Proben mit diesen Bakterien, umfassend die Schritte a) der in vitro-Zugabe der biologischen Probe zum %Helicobacter%-Bakterium gemas Anspruch 4 und b) des Screenings auf Antikörperbindung des %Helicobacter%-Bakteriums oder eines Fragments davon.

14. Ein diagnostischer Immunoassay-Kit zur Detektion der Produktion von Antikörpern gegen %Helicobacter%-Bakterien durch einen Wirt oder zur Detektion von %Helicobacter%-Bakterien, welche das %Helicobacter%-Bakterium gemas Anspruch 4 umfassen.
15. Eine Methode zur Produktion von anti-%Helicobacter%-Antikörpern beim Tier, umfassend den Gebrauch einer effektiven Menge eines Immunogens, umfassend das %Helicobacter%-Bakterium gemas Anspruch 4, worin die anti-%Helicobacter%-Antikörper an das genannte %Helicobacter%-Bakterium oder eine seiner Komponenten binden.
16. Ein Immunogen, umfassend das %Helicobacter%-Bakterium gemas Anspruch 4, zur Stimulation einer Immunreaktion bei Lebewesen, wobei das genannte Immunogen dem Lebewesen verabreicht werden muss und die genannte Immunreaktion bei diesem Lebewesen %Helicobacter%-Infektionen oder -Krankheiten verhindert, schwächt oder heilt.

...CLAIMS B1

1. Une methode de production de bacteries %Helicobacter% pylori ou %Helicobacter% felis ayant des proprietes antigeniques accrues qui consiste en une culture des bacteries %Helicobacter% in vitro dans un milieu de culture d'infusion de coeur-cerveille enrichi de serum...

...antigene immunogene compare aux proprietes antigeniques des bacteries issues d'une culture de l'espece %Helicobacter% dans un milieu de culture d'infusion de coeur-cerveille enrichi de serum de veau...

...sel biliaire glycocholate.

3. La methode decrite dans la revendication n(degree) 3 ou ledit %Helicobacter% est de la souche %Helicobacter% pylori, NB3-2 ayant le numero d'accession ATCC 55714 ou G1-4 ayant le numero d'accession %55713%.
4. Une bacterie %Helicobacter% pylori ou %Helicobacter% felis ayant des proprietes antigeniques accrues qui peut etre obtenue par une culture in vitro de la bacterie %Helicobacter% dans un milieu de culture d'infusion de coeur-cerveille enrichi de serum de veau...

...un nouvel antigene immunogene compare aux proprietes antigeniques de bacteries issues d'une culture de %Helicobacter% dans un milieu de culture d'infusion de coeur-cerveille enrichi de serum de veau.

5. La bacterie %Helicobacter% selon la revendication n(degree) 4 ou les conditions comprennent 0,05 % de glycocholate de sodium.
6. La bacterie %Helicobacter% selon la revendication n(degree) 4 ou ledit %Helicobacter% est de la souche %Helicobacter% pylori, NB3-2 ayant le numero d'accession ATCC 55714 ou G1-4 ayant le numero d'accession %55713%.
7. Un vaccin comprenant la bacterie %Helicobacter% de la revendication n(degree) 4 et comprenant egalement un support ou diluant acceptable du...

...vue pharmaceutique.

8. Le vaccin selon la revendication n(degree) 7 dans lequel ladite bacterie %Helicobacter% est inactivee.
9. Le vaccin selon la revendication n(degree) 8 dans lequel ladite bacterie %Helicobacter% est inactivee par un traitement au formaldéhyde.
10. Le vaccin selon la revendication n(degree)...

...methode pour analyser un agent antimicrobien potentiel comprenant, la mise en contact de la bacterie %Helicobacter% de la revendication n(degree) 4 in vitro avec ledit agent et l'analyse des effets bactericides ou bacteriostatiques dudit agent sur la bacterie

%Helicobacter%.

13. Une methode pour detecter les anticorps d'un hote anti bacteries %Helicobacter% chez un animal ou un prelevement biologique de celui-ci, comprenant les etapes suivantes : a) la mise en contact dudit prelevement biologique avec la bacterie %Helicobacter% de la revendication n(degree) 4 in vitro et b) la recherche de la liaison de l'anticorps a la bacterie %Helicobacter% ou un fragment de celle-ci.
14. Un kit de dosage immunologique diagnostic pour detecter la production d'anticorps d'un hote anti bacteries %Helicobacter% ou pour detecter les bacteries %Helicobacter%, comportant la bacterie %Helicobacter% de la revendication n(degree) 4.
15. Une methode de production d'anticorps anti-%Helicobacter% chez un animal non humain qui comprend l'utilisation d'une quantite efficace d'un immunogene comportant la bacterie %Helicobacter% de la revendication n(degree) 4, dans lequel les anticorps anti-%Helicobacter% se fixent sur la bacterie %Helicobacter% ou sur un fragment de celle-ci.
16. Un immunogene comprenant la bacterie %Helicobacter% de la revendication n(degree) 4, pour stimuler une reponse immunitaire chez un animal ou...

...administre a l'animal et ladite reponse immunitaire previent, attenuée ou guerit les infections a %Helicobacter% ou les maladies chez l'animal.

1/3,KWIC/3 (Item 1 from file: 340)
DIALOG(R)File 340:CLAIMS(R)/US Patent
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3140596 3959399

CM/VACCINES COMPRISING ENHANCED ANTIGENIC %HELICOBACTER% SPP.

Inventors: Frey Steven Michael (US); Pace John Lee (US); Walker Richard Ives (US)

Assignee: Antex Biologics Inc

Assignee Code: 36041

(REASSIGNED - See file 123 for details)

Attorney, Agent or Firm: Pennie & Edmonds

	Publication Number	Kind	Date	Application Number	Date
	US 5897475	A	19990427	US 95538544	19951003
	(Cited in 002 later patents)				
Cont.-in-part of:	Abandoned			US 94318409	19941005
Priority Applic:				US 95538544	19951003
				US 94318409	19941005

Calculated Expiration: 20141005

VACCINES COMPRISING ENHANCED ANTIGENIC %HELICOBACTER% SPP.

Abstract: ...containing the enteric bacteria. Specifically, a whole enteric bacteria or components thereof are provided by %Helicobacter% species. Also there are other enteric bacteria which are useful for the disclosed invention; such...

Exemplary Claim:

D R A W I N G

1. A vaccine comprising a %Helicobacter% bacterium having an enhanced antigenic property or an immunogenic fragment of said bacterium, which bacterium is harvested from a liquid culture of a %Helicobacter% species grown in vitro in a culture medium with a combination of conditions comprising: a...

...to about 100 mu M of ethylene-bis(oxyethylenenitrilo)-tetraacetic acid/acetoxymethyl ester, wherein said %Helicobacter% culture is at about early log phase, between early log phase and stationary phase, or ...

...host cell when compared to the adherence ability of bacteria from a culture of the %Helicobacter% species grown in brain heart infusion broth supplemented with bovine calf serum.

Non-exemplary Claims:

2. A vaccine comprising a %Helicobacter% bacterium having an enhanced antigenic property or an immunogenic fragment of said bacterium, which bacterium is harvested from a liquid culture of a %Helicobacter% species grown in vitro in a culture medium with a combination of conditions comprising: a...

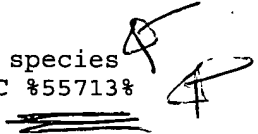
...20% CO sub 2 with about 70% to about 85% N sub 2, wherein said %Helicobacter% culture is at about early log phase, between early log phase and stationary phase, or...

...host cell when compared to the adherence ability of bacteria from a culture of the %Helicobacter% species grown in brain heart infusion broth supplemented with bovine calf serum...

...4. The vaccine according to claim 1 or 2, wherein said %Helicobacter% bacterium is inactivated...

...5. The vaccine according to claim 4, wherein said %Helicobacter% bacterium is inactivated by formalin treatment...

...8. The vaccine according to claim 1, wherein the %Helicobacter% species is %Helicobacter% pylori or %Helicobacter% felis...

...9. The vaccine according to claim 8, wherein the %Helicobacter% species is %Helicobacter% pylori strain NB3-2 (ATCC 55714) or G1-4 (ATCC %55713%)


...11. The vaccine according to claim 10, wherein the %Helicobacter% species is %Helicobacter% pylori or %Helicobacter% felis.

1/3,KWIC/4 (Item 1 from file: 654)
DIALOG(R)File 654:US Pat.Full.
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4138424

Derwent Accession: 1996-209839

Utility

REASSIGNED

CM/ Vaccines comprising enhanced antigenic %helicobacter% spp.

Inventor: Pace, John Lee, Germantown, MD

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Frey, Steven Michael, Germantown, MD

Assignee: Antex Biologics, Inc.(02), Gaithersburg, MD

Antex Biologics Inc (Code: 36041)

Examiner: Wityshyn, Michael G. (Art Unit: 188)

Assistant Examiner: Ware, Deborah

Law Firm: Pennie & Edmonds

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 5897475	A	19990427	US 95538544	19951003
CIP	Abandoned			US 94318409	19941005

Fulltext Word Count: 15997

Vaccines comprising enhanced antigenic %helicobacter% spp.

Abstract:

...containing the enteric bacteria. Specifically, a whole enteric bacteria or components thereof are provided by %Helicobacter% species. Also there are other enteric bacteria which are useful for the disclosed invention; such...

Summary of the Invention:

...method for producing enteric bacteria selected from the group consisting of Campylobacter spp., Yersinia spp., %Helicobacter% spp., Gastrospirillum spp., Bacteroides spp., Klebsiella spp., Enterobacter spp., Salmonella spp., Shigella spp., Aeromonas spp...

...the invention is enteric bacteria selected from the group consisting of Campylobacter spp., Yersinia spp., %Helicobacter% spp., Gastrospirillum spp., Bacteroides spp., Klebsiella spp., Enterobacter spp., Salmonella spp., Shigella spp., Aeromonas spp...

...enteric bacteria or components thereof, selected from the group consisting of: Campylobacter spp., Yersinia spp., %Helicobacter% spp., Gastrospirillum spp., Bacteroides spp., Klebsiella spp., Enterobacter spp., Salmonella spp., Shigella spp., Aeromonas spp...

...bacteria having enhanced antigenic properties selected from the group consisting of: Campylobacter spp., Yersinia spp., %Helicobacter% spp., Gastrospirillum spp., Bacteroides spp., Klebsiella spp., Enterobacter spp., Salmonella spp., Shigella spp., Aeromonas spp...

...invention having enhanced antigenic properties selected from the group consisting of: Campylobacter spp., Yersinia spp., %Helicobacter% spp., Gastrospirillum spp., Bacteroides spp., Klebsiella spp., Enterobacter spp., Salmonella spp., Shigella spp., Aeromonas spp...

...bacteria having enhanced antigenic properties selected from the group consisting of: Campylobacter spp., Yersinia spp., %Helicobacter% spp., Gastrospirillum spp., Bacteroides spp., Klebsiella spp., Enterobacter spp., Salmonella spp., Shigella spp., Aeromonas spp...

...enterocolitica, Yersinia pestis, Yersinia pseudotuberculosis, Escherichia coli, Shigella flexneri, Shigella sonnei, Shigella dysenteriae, Shigella boydii, %Helicobacter% pylori, %Helicobacter% felis, Gastrospirillum hominus, Vibrio cholerae, Vibrio parahaemolyticus, Vibrio vulnificus, Bacteroides fragilis, Clostridium difficile, Salmonella typhimurium...

Description of the Drawings:

...FIG. 12 graphically depicts the effect of bile concentration and the growth phase of the %Helicobacter% pylori culture on the adhesiveness of %Helicobacter% pylori NB3-2 cells. H. pylori NB3-2 cells were grown in culture medium containing...

...FIG. 13 graphically depicts the effect of bile concentration and the growth phase of the %Helicobacter% pylori culture on the adhesiveness of %Helicobacter% pylori G1-4 cells. H. pylori G1-4 cells were grown in culture medium containing...

Description of the Invention:

...the present invention, enteric bacterial cultures selected from the group of Campylobacter spp., Yersinia spp., %Helicobacter% spp., Gastrospirillum spp., Bacteroides spp., Klebsiella spp., Enterobacter spp., Salmonella spp., Shigella spp., aeromonas spp...

- ...N₂ (microaerophilic condition, "MC") for 20 h. Stocks of *Escherichia coli*, *Salmonella typhimurium*, *Helicobacter pylori* and *Shigella flexneri* can be prepared by growing the organism in brain heart infusion...
- ...In further preferred embodiments, antigenically enhanced cells of *Helicobacter pylori*, preferably of the strain ATCC 49503, NB3-2 or G1-4, are grown in...
- ...et al. (see infra Section 13) is used to assess virulence and vaccine efficacy. With *Helicobacter pylori*, the *Helicobacter felis* gastric colonization model described by Chen et al. (Lancet, 339:1120-1121, 1992) is...*Helicobacter pylori* was added to BHI broth plus 4% bovine calf serum. After inoculation the flasks...
- ...*Helicobacter pylori* was added to BHI broth plus 4% bovine calf serum. After inoculation the flasks...
- ...the bacteria were prepared as follows. For slow growing enteric bacteria such as *Campylobacter* and *Helicobacter* the bacterial culture density was diluted to an OD₆₂₅ of 0.1 with...
- ...enhancement or alteration by bile or bile salts such as DOC (e.g., *Campylobacter*, *Shigella*, *Helicobacter*) have genes homologous to low calcium response (lcr) genes from *Yersinia*. The lcr locus is...Vaccine Efficacy of *Helicobacter* Grown According to the Methods of the Present Invention...
- ...The protective efficacy of formalin-fixed whole cell *Helicobacter pylori* grown according to the methods of the present invention was determined using the mouse *Helicobacter felis* gastric colonization model described by Chen et al. (Lancet, 339:1120-1121, 1992). *Helicobacter pylori* strain G1-4 was grown as a seed culture for about 22 h at...
- ...of this inactivated whole cell vaccine orally to 6-8 week old female Balb/c *Helicobacter*-free mice at days 0, 7 and 14 or at days 0, 7 and 21...
- ...As shown in Table 20, administration of enhanced *Helicobacter* whole cell vaccine prepared using *H. pylori* strain G1-4 protected animals against an H...

Exemplary or Independent Claim(s):

1. A vaccine comprising a *Helicobacter* bacterium having an enhanced antigenic property or an immunogenic fragment of said bacterium, which bacterium is harvested from a liquid culture of a *Helicobacter* species grown in vitro in a culture medium with a combination of conditions comprising...
 - ...wherein said *Helicobacter* culture is at about early log phase, between early log phase and stationary phase, or...
 - ...host cell when compared to the adherence ability of bacteria from a culture of the *Helicobacter* species grown in brain heart infusion broth supplemented with bovine calf serum.

Non-exemplary or Dependent Claim(s):

2. A vaccine comprising a *Helicobacter* bacterium having an enhanced antigenic property or an immunogenic fragment of said bacterium, which bacterium is harvested from a liquid culture of a *Helicobacter* species grown in vitro in a culture medium with a combination of conditions comprising...
 - ...wherein said *Helicobacter* culture is at about early log phase, between

early log phase and stationary phase, or...

...host cell when compared to the adherence ability of bacteria from a culture of the %Helicobacter% species grown in brain heart infusion broth supplemented with bovine calf serum...

...4. The vaccine according to claim 1 or 2, wherein said %Helicobacter% bacterium is inactivated...

...5. The vaccine according to claim 4, wherein said %Helicobacter% bacterium is inactivated by formalin treatment...

...8. The vaccine according to claim 1, wherein the %Helicobacter% species is %Helicobacter% pylori or %Helicobacter% felis...

...9. The vaccine according to claim 8, wherein the %Helicobacter% species is %Helicobacter% pylori strain NB3-2 (ATCC 55714) or G1-4 (ATCC %55713%).

...11. The vaccine according to claim 10, wherein the %Helicobacter% species is %Helicobacter% pylori or %Helicobacter% felis.

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? s ((gl (n) 4) or gl-4) (25n) (helicobact? or pylori or pyloris or pyloridis
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        1 348: EUROPEAN PATENTS_1978-2006/ 200630
        1 349: PCT FULLTEXT_1979-2006/UB=20060727,UT=20060720
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N2	1	348: EUROPEAN PATENTS_1978-2006/ 200630
N3	1	349: PCT FULLTEXT_1979-2006/UB=20060727,UT=20060720
N4	1	654: US Pat.Full._1976-2006/Jul 27
N5	0	2: INSPEC_1898-2006/Jul W4
N6	0	5: Biosis Previews(R)_1969-2006/Jul W4
N7	0	6: NTIS_1964-2006/Jul W3
N8	0	8: Ei Compendex(R)_1970-2006/Jul W4
N9	0	9: Business & Industry(R)_Jul/1994-2006/Jul 28
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File 348:EUROPEAN PATENTS 1978-2006/ 200630

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DERWENT-ACC-NO: 1996-209839
 DERWENT-WEEK: 200643
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TITLE: Prod'n. of antigenically enhanced Helicobacter species - using cultures which simulate in vivo conditions, for prepn. of antibodies and vaccines

INVENTOR: FREY, S M; PACE, J L ; WALKER, R I

PATENT-ASSIGNEE: ANTEX BIOLOGICS INC (ANTEN), MICROCARB INC (MICRN),
 EMERGENT IMMUNOSOLUTIONS INC (EMERN)

PRIORITY-DATA: 1995US-0538544 (October 3, 1995), 1994US-0318409 (October 5, 1994), 1997US-0865147 (May 29, 1997), 1995US-0538543 (October 3, 1995), 1995US-0538545 (October 3, 1995)

Search Selected

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PATENT-FAMILY:

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<input type="checkbox"/> <u>WO 9611257 A1</u>	April 18, 1996	E	089	C12N001/00
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DESIGNATED-STATES: AL AM AU BB BG BR BY CA CN CZ EE FI GE HU IS JP KG KP KR KZ
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CITED-DOCUMENTS:6.Jnl.Ref

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
ES 2255064T3	October 4, 1995	1995EP-0937405	
ES 2255064T3		EP <u>792347</u>	Based on
WO 9611257A1	October 4, 1995	1995WO-US12986	
AU 9539527A	October 4, 1995	1995AU-0039527	
AU 9539527A		WO 9611257	Based on
NO 9701518A	October 4, 1995	1995WO-US12986	
NO 9701518A	April 3, 1997	1997NO-0001518	
FI 9701402A	October 4, 1995	1995WO-US12986	
FI 9701402A	April 4, 1997	1997FI-0001402	
EP 792347A1	October 4, 1995	1995EP-0937405	
EP 792347A1	October 4, 1995	1995WO-US12986	
EP 792347A1		WO 9611257	Based on
CZ 9701042A3	October 4, 1995	1995WO-US12986	
CZ 9701042A3	October 4, 1995	1997CZ-0001042	
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BR 9509275A	October 4, 1995	1995WO-US12986	
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JP 10507346W	October 4, 1995	1996JP-0512682	
JP 10507346W		WO 9611257	Based on
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HU 77574T	October 4, 1995	1998HU-0000341	
HU 77574T		WO 9611257	Based on
KR 97706386A	October 4, 1995	1995WO-US12986	
KR 97706386A	April 7, 1997	1997KR-0702257	

KR 97706386A		WO 9611257	Based on
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NZ 295877A	October 4, 1995	1995WO-US12986	
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SG 73510A1	October 4, 1995	1998SG-0000819	
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MX 202889B	April 3, 1997	1997MX-0002432	
SG 90030A1	October 4, 1995	1998SG-0000692	
CN 1169751A	October 4, 1995	1995CN-0196594	
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KR 422055B	October 4, 1995	1995WO-US12986	
KR 422055B	April 7, 1997	1997KR-0702257	
KR 422055B		KR 97706386	Previous Publ.
KR 422055B		WO 9611257	Based on
JP 3635580B2	October 4, 1995	1995WO-US12986	
JP 3635580B2	October 4, 1995	1996JP-0512682	
JP 3635580B2		JP 10507346	Previous Publ.
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EP 792347B1	October 4, 1995	1995EP-0937405	
EP 792347B1	October 4, 1995	1995WO-US12986	
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DE 69534635E	October 4, 1995	1995DE-0634635	
DE 69534635E	October 4, 1995	1995EP-0937405	
DE 69534635E	October 4, 1995	1995WO-US12986	

DE 69534635E

EP 792347

Based on

DE 69534635E

WO 9611257

Based on

73509 A1 INT-CL (IPC): A01N 63/00; A61K 39/00; A61K 39/02; A61K 39/106; A61K 39/38; A61K 45/00; C12N 0/00; C12N 1/00; C12N 1/12; C12N 1/20; C12Q 1/02; G01N 33/15; G01N 33/531; G01N 33/569; C12N 1/20; C12R 1/01

RELATED-ACC-NO: 1996-209840

ABSTRACTED-PUB-NO: US 5897475A

BASIC-ABSTRACT:

Prod. of *Helicobacter* bacteria having enhanced antigenic properties comprises growing a culture of the bacteria in vitro under the following conditions, either: (a) 0.05-3% bile or 0.0-25 to 0.6% of one or more bile acids or salts; (b) temp. of 30-42 deg. C; (c) in air or microaerophilic conditions comprising: (i) 5-20% carbon dioxide, 80-95% air, or (ii) 5-10% oxygen, 10-20% CO₂, 70-85% nitrogen, and (d) divalent cation chelator selected from 0-100 mu M BAPTA/AM, 0-10 mM EGTA or 0-100 mu M EGTA/AM, or: (a) divalent cation chelator selected from 1.0-25 mu M BAPTA/AM, 0.5-10 mM EGTA and 1.0-100 mu M EGTA/AM, and (b) (b) and (c) as above. The bacteria is cultured for sufficient time to reach a growth phase at approx early log phase, between early log phase and stationary phase, or at stationary phase.

USE - The bacteria can be used to produce protective vaccines, for diagnostic purposes, e.g. for the prodn. of antibodies and detection of pathogenic enteric bacteria, or to produce antibiotics. The antibodies induced by the bacteria may be used as passive vaccines.

ADVANTAGE - The bacteria produced are antigenically enhanced with phenotypic changes such as increased total protein/cell, new or increased individual proteins, altered or increased surface carbohydrates, altered lipopolysaccharides, increased adhesive ability, increased invasive ability and/or increased intracellular swarming. These enhanced bacteria induce immune responses that are cross-protective against a broader range of strains or serotypes of the same species than those induced by the same bacteria cultured under conventional conditions. The methods are adaptable to practical scale-up fermentations for commercial use.

ABSTRACTED-PUB-NO: US 6051416A

EQUIVALENT-ABSTRACTS:

Prod. of *Helicobacter* bacteria having enhanced antigenic properties comprises growing a culture of the bacteria in vitro under the following conditions, either: (a) 0.05-3% bile or 0.0-25 to 0.6% of one or more bile acids or salts; (b) temp. of 30-42 deg. C; (c) in air or microaerophilic conditions comprising: (i) 5-20% carbon dioxide, 80-95% air, or (ii) 5-10% oxygen, 10-20% CO₂, 70-85% nitrogen, and (d) divalent cation chelator selected from 0-100 mu M BAPTA/AM, 0-10 mM EGTA or 0-100 mu M EGTA/AM, or: (a) divalent cation chelator selected from 1.0-25 mu M BAPTA/AM, 0.5-10 mM EGTA and 1.0-100 mu M EGTA/AM, and (b) (b) and (c) as above. The bacteria is cultured for sufficient time to reach a growth phase at approx early log phase, between early log phase and stationary phase, or at stationary phase.

USE - The bacteria can be used to produce protective vaccines, for diagnostic purposes, e.g. for the prodn. of antibodies and detection of pathogenic enteric bacteria, or to produce antibiotics. The antibodies induced by the bacteria may be used as passive vaccines.

ADVANTAGE - The bacteria produced are antigenically enhanced with phenotypic changes such as increased total protein/cell, new or increased individual proteins, altered or increased surface carbohydrates, altered lipopolysaccharides, increased adhesive ability, increased invasive ability and/or increased intracellular swarming. These enhanced bacteria induce immune responses that are cross-protective against a broader range of strains or serotypes of the same species than those induced by the same bacteria cultured under conventional conditions. The methods are adaptable to practical scale-up fermentations for commercial use.

Prod'n. of *Helicobacter* bacteria having enhanced antigenic properties comprises growing a culture of the bacteria in vitro under the following conditions, either: (a) 0.05-3% bile or 0.0-25 to 0.6% of one or more bile acids or salts; (b) temp. of 30-42 deg. C; (c) in air or microaerophilic conditions comprising: (i) 5-20% carbon dioxide, 80-95% air, or (ii) 5-10% oxygen, 10-20% CO₂, 70-85% nitrogen, and (d) divalent cation chelator selected from 0-100 μ M BAPTA/AM, 0-10 mM EGTA or 0-100 μ M EGTA/AM, or: (a) divalent cation chelator selected from 1.0-25 μ M BAPTA/AM, 0.5-10 mM EGTA and 1.0-100 μ M EGTA/AM, and (b) (b) and (c) as above. The bacteria is cultured for sufficient time to reach a growth phase at approx early log phase, between early log phase and stationary phase, or at stationary phase.

USE - The bacteria can be used to produce protective vaccines, for diagnostic purposes, e.g. for the prod'n. of antibodies and detection of pathogenic enteric bacteria, or to produce antibiotics. The antibodies induced by the bacteria may be used as passive vaccines.

ADVANTAGE - The bacteria produced are antigenically enhanced with phenotypic changes such as increased total protein/cell, new or increased individual proteins, altered or increased surface carbohydrates, altered lipopolysaccharides, increased adhesive ability, increased invasive ability and/or increased intracellular swarming. These enhanced bacteria induce immune responses that are cross-protective against a broader range of strains or serotypes of the same species than those induced by the same bacteria cultured under conventional conditions. The methods are adaptable to practical scale-up fermentations for commercial use.

WO 9611257A

CHOSEN-DRAWING: Dwg.12,13/

DERWENT-CLASS: B04 C07 D16 S03

CPI-CODES: B01-D01; B04-B04D4; B04-F10A; B04-G01; B11-C07A; B12-K04A4; B14-A01A; D05-A01A4; D05-A01B; D05-C02; D05-H04; D05-H07; D05-H09; D05-H11A1;

EPI-CODES: S03-E14H4;